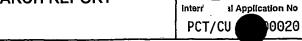
INTERNATIONAL SEARCH REPORT



| A. CLASSII | ICATION OF SUBJEC | CT MATTER |
|------------|-------------------|-----------|
| IPC 7 | A61K9/02 | A61K38/49 |

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

 $\begin{tabular}{ll} Minimum documentation searched (classification system followed by classification symbols) \\ IPC 7 & A61K \end{tabular}$

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

WPI Data, PAJ, MEDLINE, EMBASE, BIOSIS, EPO-Internal

| Category ° | Citation of document, with indication, where appropriate, of the | relevant necsanes | Relevant to claim No. |
|--|--|--|---|
| | Citation of document, with indication, where appropriate, or the | Televant passages | THE TAIN TO CLAME TO |
| X | EP 0 672 659 A (LILLY CO ELI) 20 September 1995 (1995-09-20) | | 1 |
| | page 40, line 38 - line 49 | | |
| X | EP 0 340 933 A (BIOPHARM CLINIC LIM) 8 November 1989 (1989-11-6 page 2, line 47 page 3, line 21 - line 30 | | 1 |
| X | US 6 440 947 B1 (BARRON HAL V 27 August 2002 (2002-08-27) column 2, line 66 - line 67 column 13, line 5 - line 8 | ET AL) | 1,2 |
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| X Furth | er documents are listed in the continuation of box C. | X Patent family members are listed in | n annex. |
| | | | |
| A* docume: | egories of cited documents : nt defining the general state of the art which is not exert to be of particular relevance. | "T" later document published after the Inte- or priority date and not in conflict with cited to understand the principle or the | the application but |
| A" docume: conside E" earlier d | nt defining the general state of the art which is not ered to be of particular relevance ocument but published on or after the International | or priority date and not in conflict with cited to understand the principle or the invention "X" document of particular relevance; the c | the application but cory underlying the laimed invention |
| A" docume conside E" earlier d filing de L" documer which le | nt defining the general state of the art which is not extend to be of particular relevance ocument but published on or after the international ate at which may throw doubts on priority claim(s) or so clied to establish the publication date of another | or priority date and not in conflict with cited to understand the principle or the invention "X" document of particular relevance; the c cannot be considered novel or cannot involve an inventive step when the document of particular relevance; the c | the application but cory underlying the laimed invention be considered to cument is taken alone laimed invention |
| A" docume conside E" earlier d filling de L" documer which le citation O" docume | nt defining the general state of the art which is not ered to be of particular relevance ocument but published on or after the international ate in twhich may throw doubts on priority claim(s) or so clied to establish the publication date of another or other special reason (as specified) int referring to an oral disclosure, use, exhibition or | or priority date and not in conflict with cited to understand the principle or the invention "X" document of particular relevance; the cannot be considered novel or cannot involve an inventive step when the do "Y" document of particular relevance; the cannot be considered to involve an inventive step with the document is combined with one or mo | the application but sory underlying the laimed invention be considered to cument is taken alone laimed invention rentive step when the re other such docu- |
| A" documer conside E" earlier diffiling de L" documer which is citation other m other m documer documer documer m do | nt defining the general state of the art which is not ered to be of particular relevance ocument but published on or after the international ate nt which may throw doubts on priority claim(s) or scited to establish the publication date of another or other special reason (as specified) nt referring to an oral disclosure, use, exhibition or reans nt published prior to the international filling date but | or priority date and not in conflict with clied to understand the principle or the invention "X" document of particular relevance; the c cannot be considered novel or cannot involve an inventive step when the do document of particular relevance; the c cannot be considered to involve an inventive and the considered to involve and involve an | the application but convention by underlying the laimed invention be considered to coment is taken alone laimed invention rentive step when the re other such docusts to a person skilled |
| A" docume conside E" earlier de filing de L" documer which le citation O" docume other m documer later the | nt defining the general state of the art which is not eared to be of particular relevance ocument but published on or after the international ate of the stabilish the publication date of another or other special reason (as specified) or the referring to an oral disclosure, use, exhibition or nears | or priority date and not in conflict with cited to understand the principle or the invention "X" document of particular relevance; the c cannot be considered novel or cannot involve an inventive step when the document of particular relevance; the c cannot be considered to involve an involve and involve and involve and in the art. | the application but cory underlying the laimed invention be considered to comment is taken alone laimed invention rentive step when the re other such docusto a person skilled family |
| A* documer consider earlier diffing da L* documer which is citation of documer other more documer later that the control of the a | nt defining the general state of the art which is not eared to be of particular relevance ocument but published on or after the international ate of the stabilish the publication date of another or other special reason (as specified) or the ferring to an oral disclosure, use, exhibition or neans of prior to the international filling date-but an the priority date claimed | or priority date and not in conflict with cited to understand the principle or the invention "X" document of particular relevance; the c cannot be considered novel or cannot involve an inventive step when the document of particular relevance; the c cannot be considered to involve an important is combined with one or moments, such combined with one or moments, such combination being obvious in the art. "8" document member of the same patent of the same patent of mailing of the International sear | the application but cory underlying the laimed invention be considered to comment is taken alone laimed invention rentive step when the re other such docusto a person skilled family |
| A" documer consider a filing de L" documer which is citation or documer alter the later of the a | nt defining the general state of the art which is not ered to be of particular relevance ocument but published on or after the international ate in which may throw doubts on priority claim(s) or so clied to establish the publication date of another or other special mason (as specified) intreferring to an oral disclosure, use, exhibition or nears in published prior to the international filling date but an the priority date claimed international search | or priority date and not in conflict with cited to understand the principle or the invention "X" document of particular relevance; the c cannot be considered novel or cannot involve an inventive step when the document of particular relevance; the c cannot be considered to involve an important is combined with one or moments, such combined with one or moments, such combination being obvious in the art. "8" document member of the same patent of the same patent of mailing of the International sear | the application but sory underlying the laimed invention be considered to current is taken alone laimed invention rentive step when the re other such docurs to a person skilled family |

INTERNATIONAL SEARCH REPORT

Inte | Application No PCT/CU 10020

| | | PCT/CU | 0020 |
|------------|---|--------|-----------------------|
| C.(Continu | ation) DOCUMENTS CONSIDERED TO BE RELEVANT | | |
| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | | Relevant to claim No. |
| A | SUMI H ET AL: "Activation of plasma fibrinolysis after intrarectal administration of high molecular urokinase and its derivative." ACTA HAEMAT., vol. 70, 1983, pages 289-295, XP002903001 ISBN: 0001-5792 the whole document | | 1-20 |
| A | MACKAY M ET AL: "Peptide drug delivery: Colonic and rectal absorption." ADVANCED DRUG DELIVERY REVIEWS, vol. 28, 1997, pages 253-273, XP002903002 Elsevier Science B.V. ISBN: 0169-409X the whole document | | 1-20 |
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| Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sneet) |
|---|
| This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons: |
| 1. X Claims Nos.: 13-20. because they relate to subject matter not required to be searched by this Authority, namely: Although claim(s) 13-20 are directed to a diagnostic method practised on the |
| Although claim(s) 13-20 are directed to a diagnostic method probabilities and based on the alleged human/animal body, the search has been carried out and based on the alleged effects of the compound/composition. |
| 2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: |
| |
| 3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). |
| Box II Observations where unity of Invention is lacking (Continuation of item 2 of first sheet) |
| This International Searching Authority found multiple inventions in this international application, as follows: |
| see additional sheet |
| |
| As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims. |
| 2. X As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee. |
| 3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.: |
| 4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: |
| Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees. |

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

- 1. Claims: 3, 4, 14, 18 and (1, 2, 7-13, 15-17) partially Formulation containing streptokinase for rectal administration.
- 2. Claims: 5, 15, 19 and (1, 2, 7-13, 15-17) partially Formulation containing urokinase for rectal administration.
- 3. Claims: 6, 16, 20 and (1, 2, 7-13, 15-17) partially

 Formulation containing plasminogen tissue activator for rectal administration.

INTERNATIONAL SEARCH REPORT

| | ŢŲ. | on on patent family men | nbers | , Р | CT/C /00020 |
|--|-----|-------------------------|--|--|---|
| Patent document cited in search report | | Publication date | | Patent family member(s) | Publication date |
| EP 0672659 | A | 20-09-1995 | US AT CA DE DE DK EP ES GR JP SI US | 175404 2143536 69507062 69507062 672659 0672659 2126211 3029389 7258287 672659 6124277 | T1 30-04-1999 |
| EP 0340933 | Α | 08-11-1989 | AT AU DE DE EP EP WO JP US | 632482 3444589 68908716 68908716 0340933 0440625 2058601 8909615 | T 15-09-1993 B2 07-01-1993 A 03-11-1989 D1 30-09-1993 T2 14-07-1994 A2 08-11-1989 A1 14-08-1991 T3 01-11-1994 A1 19-10-1989 B2 06-08-1998 T 15-08-1991 A 18-01-1994 |
| US 6440947 | B1 | 27-08-2002 | US AU CA EP JP WO | | A1 26-07-2000 T 18-02-2003 |

Application No

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INFORME DE BUSQUEDA INTERNACIONAL

| I | Solid | iternacional N° |
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| | PCT/0 | /00020 |

A. CLASIFICACION DE LA INVENCION CIP 7 A61K9/02 A61K38/49

Según la clasificación internacional de patentes (CIP) o según la clasificación nacional y la CIP

B. SECTORES COMPRENDIDOS POR LA BUSQUEDA

Documentación mínima consultada (sistema de clasificación seguido de los símbolos de clasificación)

CIP 7 A61K

Otra documentación consultada además de la documentación mínima en la medida en que tales documentos forman parte de los sectores comprendidos por la búsqueda

Base de datos electrónica consultada durante la búsqueda internacional (nombre de la base de datos, y cuando sea aplicable, términos de búsqueda utilizados)

| Categoría° | NTOS CONSIDERADOS PERTINENTES Identificación del documento, con indicación, cuando se adecuado, de los pasajes pertinentes | N° de las reivindicaciones pertinentes |
|------------|---|---|
| Х | EP 0 672 659 A (LILLY CO ELI) 20 Septiembre 1995 (1995-09-20) página 40, línea 38 - línea 49 | 1 |
| X | EP 0 340 933 A (BIOPHARM CLINICAL RESEARCH LIM) 8 Noviembre 1989 (1989–11–08) página 2, línea 47 página 3, línea 21 – línea 30 | 1 |
| X | US 6 440 947 B1 (BARRON HAL V ET AL) 27 Agosto 2002 (2002-08-27) columna 2, linea 66 - linea 67 columna 13, linea 5 - linea 8 | 1,2 |
| Y En la | a continuación del Recuadro C se relacionan X Véase el Anexo de la famil mentos adicionales | lia de patentes. |

| Categorías especiales de documentos citados: "A" documento que define el estado general de la técnica, no considerado como particularmente pertinente "E" documento anterior, publicado ya sea en la fecha de presentación internacional o con posteriordad a la misma "L" documento que puede plantear dudas sobre reivindicación(es) de prioridad o que se cita para determinar la fecha de publicación de otra cita o por una razón especial (como la especificada) "O" documento que se reflere a una divulgación oral, a un empleo, a una exposición o a cualquier otro tipo de medio "P" documento publicado antes de la fecha de presentación internaciónal, pero con posterioridad a la fecha de prioridad reivindicada Fecha en la que se ha concluido efectivamente la búsqueda internacional | "T" documento ultarior publicado con posterioridad a la fecha de presentatión internacional o de prioridad y que no está en conflicto con la solicitud, pero que se cita para comprender el principio o la teoría que constituye la base de la Invención "X" documento de particular importancia; la invención relivindicada no puede considerarse nueva o no puede considerarse que implique actividad inventiva cuando se considera el documento aisladamente invención reinvindicada implique actividad inventiva cuando el documento esté combinado con otro u otros documentos, cuya combinación sea evidente para un experto en la materia "&" documento que forma parte de la misma familia de patentes Fecha de expedición del presente informe de búsqueda internacional 19. 04. 2004 |
|---|--|
| Nombre y dirección postal de la Administración encargada de la búsqueda internacional European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 | Funcionario autorizado M. Novoa Sanjurjo |

INFORME DE BUSQUEDA INTERNACIONAL

Solic ernacional N°
PCT/CU 9020

| | | PC1/C0 | |
|------------|--|------------------|---|
| L | ción) DOCUMENTOS CONSIDERADOS PERTINENTES | | |
| Categoria° | Identificación de los documentos citados, con indicación, cuando se adecuado, de los pasa | ijes pertinentes | N° de las reivindicaciones pertinentes |
| A | SUMI H ET AL: "Activation of plasma fibrinolysis after intrarectal administration of high molecular urokinase and its derivative." ACTA HAEMAT., vol. 70, 1983, páginas 289-295, XP002903001 ISBN: 0001-5792 el documento completo | | 1-20 |
| A | MACKAY M ET AL: "Peptide drug delivery: Colonic and rectal absorption." ADVANCED DRUG DELIVERY REVIEWS, vol. 28, 1997, páginas 253-273, XP002903002 Elsevier Science B.V. ISBN: 0169-409X el documento completo | | 1-20 |
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| Recuadro | I Observaciones cuando no han podido efectuarse búsquedas sobre ciertas reivindicaciones (continuación del punto 1 de la primera hoja) |
|-------------|--|
| | me de búsqueda internacional no se ha establecido respecto de ciertas reivindicaciones, en virtud del Artículo 17.2)a), cones siguientes: |
| 1. X | Reivindicaciones Nos.: 13-20. debido a que se refieren a objetos para los que no se ha solicitado a esta Administración su búsqueda, concretamente: |
|] | Las reivindicaciones 13 a 20 se refieren a un método diagnóstico aplicado al |
| (| cuerpo humano o animal. A pesar de ello, la búsqueda se ha realizado en |
| i | oase a los efectos atribuidos a los compuestos/a la composición. |
| | Reivindicaciones Nos.: debido a que se refieren a partes de la solicitud internacional que no cumplen con las exigencias prescritas, de forma que no puede realizarse una búsqueda internacional significativa, específicamente: |
| | Reivindicaciones Nos.: debido a que son reivindicaciones dependientes y no están redactadas de conformidad con la segunda y tercera frases de la Regla 6.4.a). |
| Recuadro | II Observaciones cuando falta la unidad de la invención (Continuación del punto 2 de la primera hoja) |
| | |
| | nistración encargada de la búsqueda internacional ha encontrado invenciones múltiples en esta solicitud internacional, indica a continuación: |
| | ver hoja suplementaria |
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| | Debido a que todas las tasas adicionales de búsqueda exigidas fueron pagadas en su momento por el solicitante, este informe de búsqueda internacional abarca todas las reivindicaciones para las que puede efectuarse la búsqueda. |
| 2. X | Debido a que puede efectuarse la búsqueda respecto de todas las reivindicaciones susceptibles de búsqueda sin esfuerzo que justifique una tase adicional, esta Administración no invita a pagar ninguna tasa adicional. |
| | Debido a que sólo algunas de las tasas adicionales de búsqueda requeridas fueron pagadas en su momento por el solicitante, este informe de búsqueda internacional abarca únicamente las reivindicaciones para las que fueron pagadas las tasas, específicamente las reivindicaciones Nos.: |
| | |
| اللا | El solicitante no pagó en su momento las tasas adicionales de búsqueda requeridas. En consecuencia, este informe de búsqueda internacional se restringe a la invención mencionada en primer lugar en las reivindicaciones; abarca las reivindicaciones Nos.: |
| | |
| | Ar A Tankan da kan and a Na and a Markan da Laskinian da |
| Observa | ción sobre protesta Las tasas de búsqueda adicional fueron acompañadas por protesta del solicitante. Ninguna protesta acompaño al pago de las tasas de búsqueda adicional. |
| | I 1 14mBana brocesa acombano at bago de tas rasas de dasdacoa accoman. |

La Administración encargada de la Búsqueda Internacional ha detectado las siguientes invenciones o los siguientes grupos de invenciones en la presente solicitud internacional:

1. reivindicaciones 3, 4, 14, 18 y (1, 2, 7-13, 15-17) parcialmente

Una formulación que contiene estreptoquinasa para la administración rectal.

2. reivindicaciones 5, 15, 19 y (1, 2, 7-13, 15-17) parcialmente

Una formulación que contiene uroquinasa para la administración rectal.

3. reivindicaciones 6, 16, 20 y (1, 2, 7-13, 15-17) parcialmente

Una formulación que contiene activador tisular del plasminógeno para la administración rectal.

INFORME DE BUSQUEDA INTERNACIONAL

iembros de la familia de patentes 00020 PCT/CU Fecha de Miembro(s) de la Fecha de Documento de patente citado publicación publicación familia de patentes en el informe de búsqueda 23-03-1999 US 20-09-1995 5885967 A Α EP 0672659 15-01-1999 175404 T ΑT 05-09-1995 2143536 A1 CA 18-02-1999 69507062 D1 DE 10-06-1999 69507062 T2 DE 17-05-1999 672659 T3 DK 20-09-1995 ΕP 0672659 A1 16-03-1999 ES 2126211 T3 28-05-1999 3029389 T3 GR 09-10-1995 7258287 A JP 30-04-1999 SI 672659 T1 26-09-2000 6124277 A US 18-07-2000 6090787 A US 15-09-1993 93393 T 08-11-1989 AT Α EP 0340933 07-01-1993 632482 B2 ΑU 03-11-1989 3444589 A ΑU 30-09-1993 68908716 D1 DE 14-07-1994 68908716 T2 DE 0340933 A2 08-11-1989 EP 14-08-1991 0440625 A1 ΕP 01-11-1994 2058601 T3 ES 19-10-1989 WO 8909615 A1 06-08-1998 2783367 B2 JP 15-08-1991 3503644 T JP 18-01-1994 US 5279824 A 26-10-1999 5972903 A US 27-08-2002 US 6440947 B1 27-04-1999 9790998 A ΑU 15-04-1999 2305726 A1 CA 26-07-2000 1021195 A1 EP 18-02-2003 2003506310 T JP 15-04-1999 9917784 A1 WO

ternacional N°

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